

In the Claims, kindly amend the following:

02

1. An expression vector comprising a vector to transform a mammary gland cell or tissue to contain a hirudin gene with an  $\alpha$ -lactoalbumin gene promoter specifically expressing nucleic acid encoding hirudin.

Kindly cancel claims 2-32 without prejudice. Please note, the cancellation of these claims was not done in response to overcome any particular rejection or objection, but instead was undertaken to preserve Applicants' rights for future prosecution of the subject matter.

## DISCUSSION

### OBJECTIONS

The July 30, 2002 Office Action requested correction of informalities under 37 CFR 1.85 as well as corrections other than informalities noted by draftsperson on form PTO-948. The drawings have been resubmitted to the draftsperson in accordance with the comments in form PTO 948 and the Office Action. Applicants respectfully request withdrawal of the objection to the drawings. In addition, the descriptive text figure 4 was amended as suggested by the Office Action to read "the Amino Acid sequence thereof" thus removing the basis for objection. Applicants respectfully request the objection to the specification be withdrawn. As claims 2-32 have been cancelled, the basis for objection to claim 20 has become moot. Applicants respectfully request that objection to the claims be withdrawn.

### THE REJECTIONS UNDER 35 U.S.C. § 112

Applicants respectfully request reconsideration of the rejection of claims 4, 7, 16, 19, 21 and 28 under 112 first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. As the rejection does not encompass the newly revised claims, this rejection is no longer applicable and Applicants respectfully request that the rejections under 35 USC first paragraph be withdrawn. Moreover, the Office Action has taken an unduly restrictive reading of 'promoter' since paragraph 27 indicates that a promoter region must only precede the desired DNA sequence, where it states "'promoter'", as used herein refer to a DNA sequence that is

located at the 5' end of (i.e., precedes)." This paragraph does not state that the promoter must start at the 5' end, but instead simply states that the promoter must be before the desired DNA sequence.

Applicants respectfully request reconsideration of the rejection of claims 6, 7, 9, 11, 14, 16-19, 27-29, 30 and 31 under 112 second paragraph for indefiniteness. As the rejection does not encompass the newly revised claims, this rejection is no longer applicable and Applicants respectfully request that the rejections under 35 USC 112 second paragraph be withdrawn.

#### **THE REJECTIONS UNDER 35 U.S.C. § 102**

The July 30, 2002 Office Action rejected claims 1,2, 5, 8, 9, 12, 13, 14 and 17 under 35 U.S.C. § 102(b) based upon US Patent Number 5,965,788 to Houdebine et al. Since claim 1 has been amended to include the  $\alpha$ -lactoalbumin gene, claim 1 includes a limitation not found within the Houdebine reference. Consequently, claim 1 cannot be anticipated by the Houdebine reference, and applicants respectfully request the rejection be withdrawn. As claims 2, 5, 8, 9, 12, 13, 14 and 17 have been cancelled, the rejection under 35 U.S.C. § 102(b) does not apply to them, and Applicants respectfully request the rejection under 35 U.S.C. § 102(b) be withdrawn.

#### **THE REJECTIONS UNDER 35 U.S.C. § 103**

Applicants respectfully request reconsideration of the combination of references cited against Applicants under 103(a). Claims 1-4, 6-11, 13-16, 18 and 19 were rejected under 35 USC 103(a) as being unpatentable over Houdebine as applied to claims 1, 2, 8, 9, 13 and 14 above and in further view of Bleck et al (WO 93/04165). As claim 1 has been amended to include an  $\alpha$ -lactoalbumin gene, discussion of the references shall be from that perspective. As the other claims have been withdrawn from prosecution, rejections directed to cancelled claims should be withdrawn as well.

Turning now to the references, unlike applicants' disclosure, no problems are indicated in Houdebine which would teach one to combine particular aspects of Houdebine with Bleck, or with any other reference for that matter. The Houdebine reference teaches the use of the rabbit WAP promoter for expression of desired proteins in transgenic mice. This central reliance on the rabbit WAP promoter would in fact teach away from selecting another

promoter for protein expression in a transgenic animal. In particular, there are no problems disclosed within Houdebine which would lead one skilled in the art to seek out another reference for the purpose of substituting an  $\alpha$ -lactoalbumin gene for the rabbit WAP promoter of Houdebine, and as such would not lead one to the Bleck reference. As stated by *Northern Telecom Inc. v. Datapoint Corp.*, 15 USPQ2d 1321, 1323,

It is insufficient that the prior art disclosed the components of the patented device, either separately or used in other combinations; there must be some teaching, suggestion, or incentive to make the combination made by the inventor. *Interconnect Planning Corp. v. Feil*, 774 F.2d 1132, 1143, 227 USPQ 543, 551 (Fed. Cir. 1988) (insufficient to select from the prior art the separate components of the inventor's combination, using the blueprint supplied by the inventor); *Rosemount, Inc. v. Beckman Instruments, Inc.*, 727 F.2d 1540, 1546, 221 USPQ 1, 7 (Fed. Cir. 1984) ("As this court has held, 'a combination may be patentable whether it be composed of elements all new, partly new or all old'") (citations omitted); *W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1551, 220 USPQ 303, 312 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984) (individual references can not be "employed as a mosaic to recreate a facsimile of the claimed invention."). The district court found that the technology for the invention claimed in the '375 patent existed at the time the invention was made, but correctly declined to engage in hindsight reconstruction of the claimed invention.

Modification of any of the disclosed elements of Houdebine detailed above would in fact teach away from the proper operation of Houdebine, since without the rabbit WAP promoter the key to the Houdebine reference would not be present. As such the reference has no bearing on the instant application, and the rejections under 35 U.S.C. § 103(a) of claim 1 should be withdrawn.

Claims 1-5, 8-17 and 32 were rejected under 35 USC 103(a) as being unpatentable over Yoo et al. (WO 00/15808) in view of Liersch et al (US patent 5,422,249). Claim 1 has now been amended to include the  $\alpha$ -lactoalbumin limitation of claim 6. Consequently, the combination of Yoo with Liersch should not apply with respect to the newly modified claim 1. Applicants respectfully request the rejection be withdrawn.

Claims 1-29 were rejected under 35 USC 103(a) as being unpatentable over Johnson (WO 98/35689) in view of Liersch. According to page 14 of the July 30, 2002 Office Action, "It would have been obvious to the skilled artisan to modify the teachings of Hwang to include the cDNA taught by Liersch for the purpose of producing hirudin from mammalian mammary

glands." For proper combination of references, the teaching to combine must stem from the references themselves, or from general knowledge of the relevant art. In this case, the motivation to combine improperly came from a third reference, where the Office Action states that "(m)otivation to combine these teachings comes from Yoo, who teaches several advantages of heterologous production of proteins in mammary glands" even though there is no teaching in Hwang which would lead one skilled in the art to seek out Yoo for purposes of combination. As the rejection of claims 1-29 under 35 U.S.C. § 103(a) was made by way of several improperly combined references, Applicants respectfully request the rejections be withdrawn in light of the newly modified claim 1.

## CONCLUSION

The Applicants respectfully assert that the presently claimed invention is patentably distinct from the cited references, and therefore requests that the present rejections be withdrawn and the instant application passed to allowance. The Examiner is cordially invited to telephone the undersigned for any reason which would advance the instant application to allowance.

Respectfully submitted,



F. David LaRiviere  
Reg. No. 27,207

FDL/rm

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LARIVIERE, GRUBMAN & PAYNE, LLP

Post Office Box 3140

Monterey, CA 93942

(831) 649-8800